REMARKS

Claims 1-57 were pending in the application. Claims 14-15, 20, 22, and 37-57 have been

cancelled as being directed to non-elected inventions. Applicants reserve the right to prosecute

these inventions in one or more continuing applications. Claims 32-36 have been cancelled

without prejudice. New claim 58 has been added. Support for the new claim can be found

throughout the claims and specification as filed. No new matter has been added.

Specification

The Examiner has objected to the specification because it contains a hyperlink on page 1,

lines 24-25. Applicants have amended the specification thereby rendering this rejection moot.

*Rejection of Claims 1-13, 16-19, 21, 23-31 and 34
Under 35 USC 112, First Paragraph*

The Examiner has indicated that claims 1-13, 16-19, 21, 23-31 and 34 are rejected under

35 USC 112, first paragraph as, allegedly, failing to comply with the enablement requirement.

Applicants respectfully traverse this rejection.

The specification provides detailed teachings regarding the claimed methods. For example

the specification teaches methods for the detection and diagnosis of cancer comprising

> detecting at least one or more protein biomarkers in a subject sample, and;
> correlating the detection of one or more protein biomarkers with a diagnosis of
> cancer, wherein the correlation takes into account the detection of one or more
> biomarker in each diagnosis, as compared to normal subjects, wherein the one or
> more protein markers are selected from Marker I (BC1); Marker II (BC2); Marker
> III (BC3); Marker IV; Marker V; Marker VII; Marker VIII; Marker IX; Marker
> X; Marker XI; Marker XII; Marker XIII; and Marker XIV, and combinations
> thereof.

> In a preferred method for detection, diagnosis and determination of the clinical
> stage of breast cancer, comprises detecting at least one or more protein
> biomarkers in a subject sample, wherein the protein markers are selected from
> Marker I (BC1); Marker II (BC2); Marker III (BC3), combinations thereof;
> and; correlating the detection of one or more protein biomarkers with a diagnosis
> of breast cancer, wherein the correlation takes into account the detection of one or
> more protein biomarkers in each diagnosis, as compared to normal subjects.

> See page 6, lines 5-20.

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The specification further provides detailed teachings regarding how to obtain biological samples from subjects and how to measure the amount of the claimed biomarkers in the sample.

Moreover, there are a number of working examples that are demonstrate that the claimed methods are enabled. For example, the specification teaches that the claimed methods demonstrate

> [t]he high specificity and sensitivity of the method used for identifying the biomarkers that differentiate between the different stages of breast cancer is underscored by using only three of these biomarkers, 4283 (BC1), 8126 (BC2) and 8932 (BC3), to correctly identify 93% of breast cancer patients at different stages: Stage 0/I (93%), stage II (85%) and stage III (94%). Using only one biomarker (BC3), correct identification 85% of breast cancer patients with stage 0/I (88%), stage II (78%) and stage III (92%) was achieved.
>
> In particular, simultaneous analysis of protein profiles of 169 serum samples of subjects with or without breast cancer using was carried out and the results demonstrate the high specificity and selectivity of the methods described herein. Out of the 169 serum samples of subjects, three discriminating biomarkers were identified, the combination of which achieved both high sensitivity (93%) and high specificity (91%) in detecting breast cancer from the non-cancer controls.

See page 25, line 14-26 of the specification.

Additionally, the Examples set forth the following tables summarize the results obtained using the identified markers. The ability of the claimed methods to accurately identify subjects having breast cancer is set forth demonstrated by the data set forth in the following tables from Examples 4 and 5.

Table 1

	Non-cancer Controls (n=66)		Breast Cancer Patients Stages 0-I (n=42)		Breast Cancer Patients Stages II-III (n=61)	
	Mean	Stdev	Mean	Stdev	Mean	Stdev
BC1	0.302	0.312	-0.118	0.244	-0.081	0.258
BC2	0.981	0.358	1.411	0.154	1.295	0.205
BC3	0.526	0.252	0.993	0.193	1.003	0.234
Comp. Index	-0.375	0.313	0.425	0.257	0.349	0.242

Table 2A. Diagnostic performance of BC3.

Cutoff=0.8	Non-Cancer Controls			Breast Cancer Patients			
				Stage			
		Benign	Subtotal	0-I	II	III	Subtotal
	0	6	6	37 (88%)	29 (78%)	22 (92%)	88 (85%)
Negative	41 (100%)	19 (76%)	60 (91%)	5	8	2	15
Total	41	25	66	42	37	24	103

Table 2B. BootStrap estimated diagnostic performance of logistic regression derived composite index using BC1, BC2 and BC3 (20 runs, leave out rate = 30%).

LR at cutoff=0	Non-Cancer Controls			Breast Cancer Patients			
				Stage			
		Benign	Subtotal	0-I	II	III	Subtotal
				93%	85%	94%	93% (85-100%)
Negative	100%	85%	91% (82 - 100%)				

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Clearly, the teachings of the specification and the extensive working examples enable the claimed methods.

The Examiner cites a number of references to support the enablement rejection, but each of these references was published *after* the priority date of the instant application. Enablement is determined *as of the effective filing date* of the patent, In re Hogan, 559 F.2d 595, 604 (CCPA 1977). The use of the post-filing references by the Examiner is improper.

While we disagree with the Examiner's characterization of these references and the teachings they provide, there is no need to address the substance of the references as they can not be properly used against the pending claims.

Accordingly, based on the extensive teachings in the specification, and the working examples, the invention is clearly enabled by the specification as filed. Applicants respectfully request that the Examiner reconsider and withdraw the foregoing rejection.

### *Rejection of Claims 32-33 and 35-36 Under 35 USC 102(b)*

The Examiner has rejected claims 32-33 and 35-36 as being anticipated by Murray et al. as evidenced by Li et al. Applicants respectfully traverse this rejection. However, while in no way acquiescing to the validity of the Examiner's rejection, and solely in the interest of expediting prosecution, Applicants have cancelled claims 32-33 and 35-36.

<u>REMARKS</u>

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Dated: February 18, 2008

Respectfully submitted
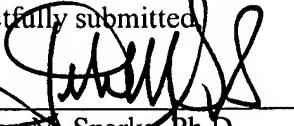
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